

(1)

Reaction scheme (1) shows the synthesis of intermediate (2) from 1,6-diaminohexane-2,5-dicarboxylic acid. The starting material is reacted with Boc anhydride in dioxane with NaOH/H₂O to form the bis-Boc-protected diamine. This intermediate is then reacted with 20 (S)-Camptothecin, DIPC, and DMAP in CH₂Cl₂ to form intermediate (2), which is a bis-Boc-protected diamine with two camptothecin units attached via ester linkages.

(2)

Reaction scheme (2) shows the deprotection of intermediate (2) using TFA/CH₂Cl₂ to yield the bis-amine intermediate (3), which has two free amine groups and two camptothecin units.

(3)

Reaction scheme (3) shows the conjugation of intermediate (3) with mPEG 20 kDa CO₂H using DIPC, DMAP, and CH₂Cl₂ to form the final mPEG-conjugated bis-amine (4).

(4)

FIG. 2

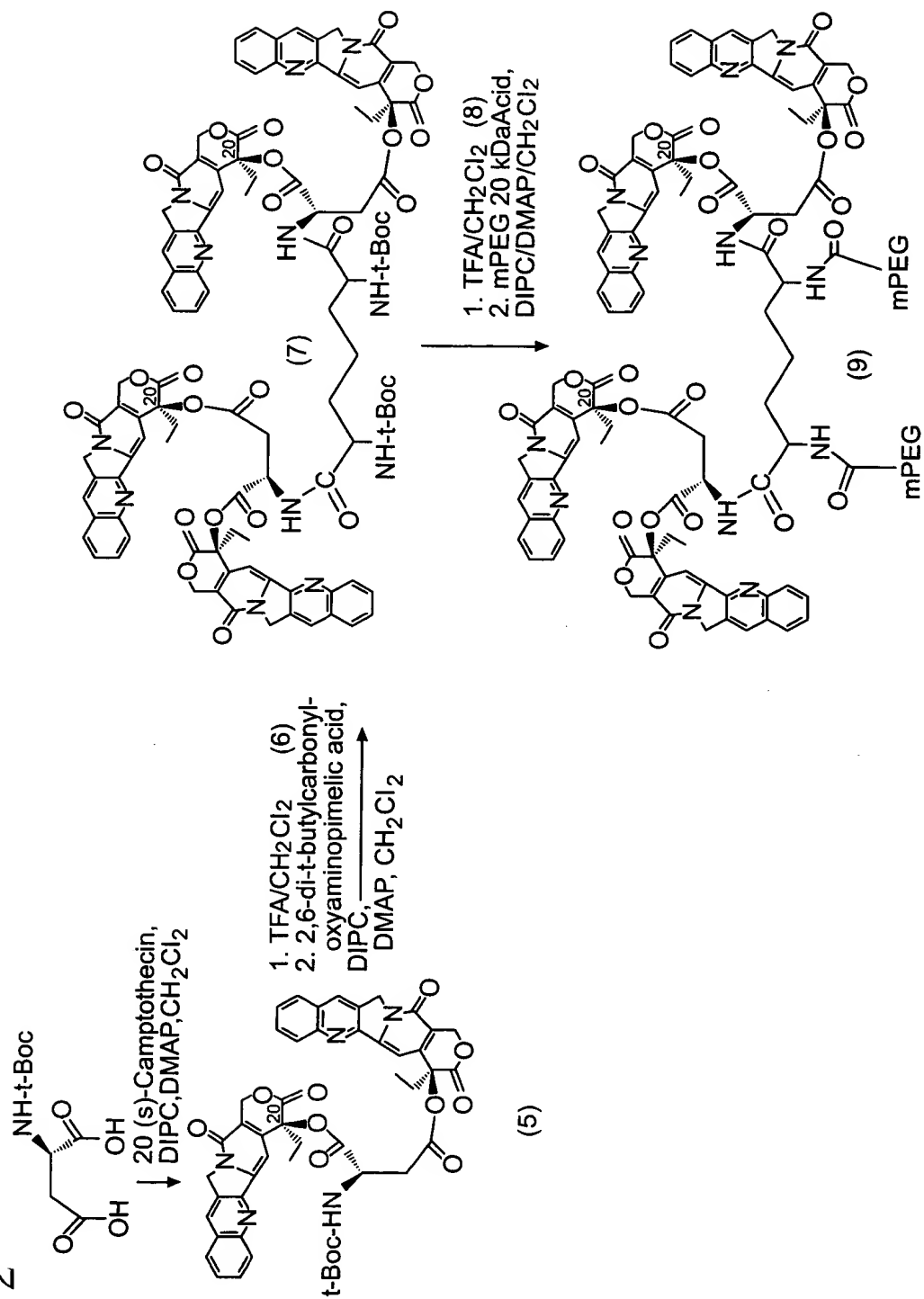
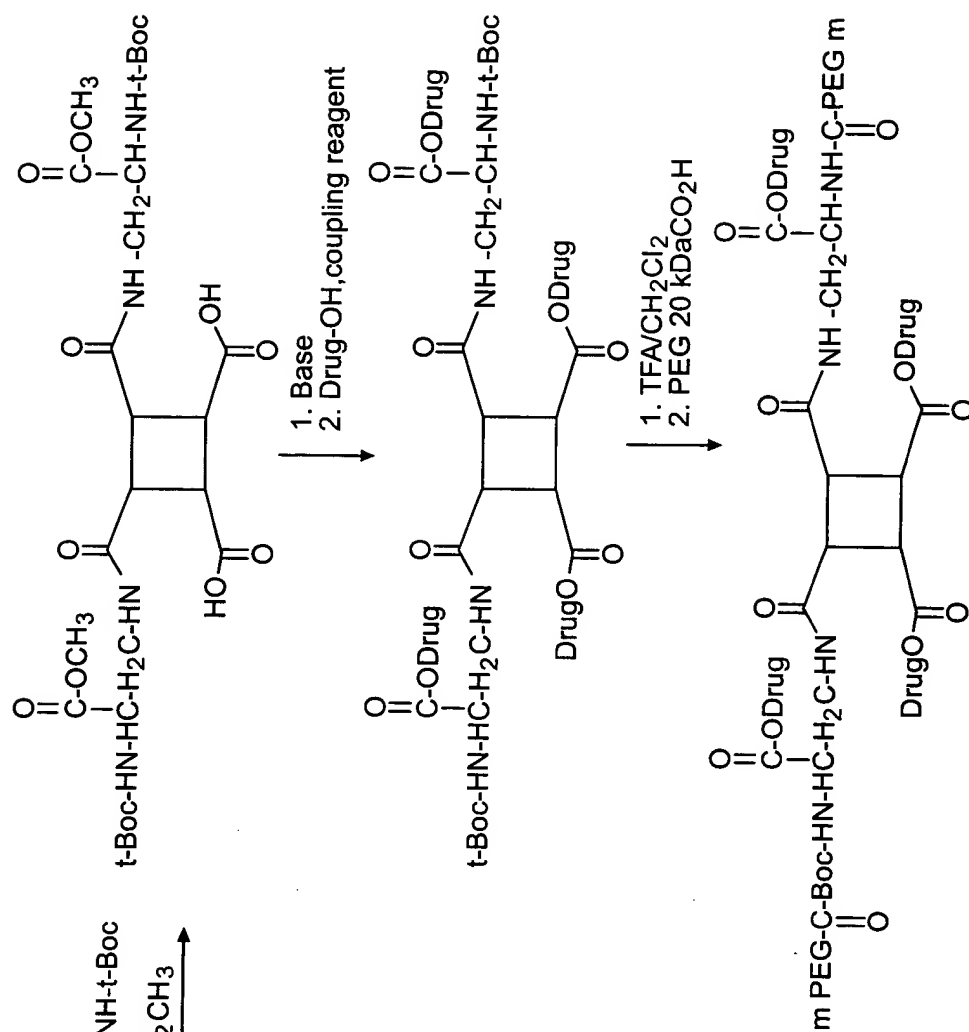
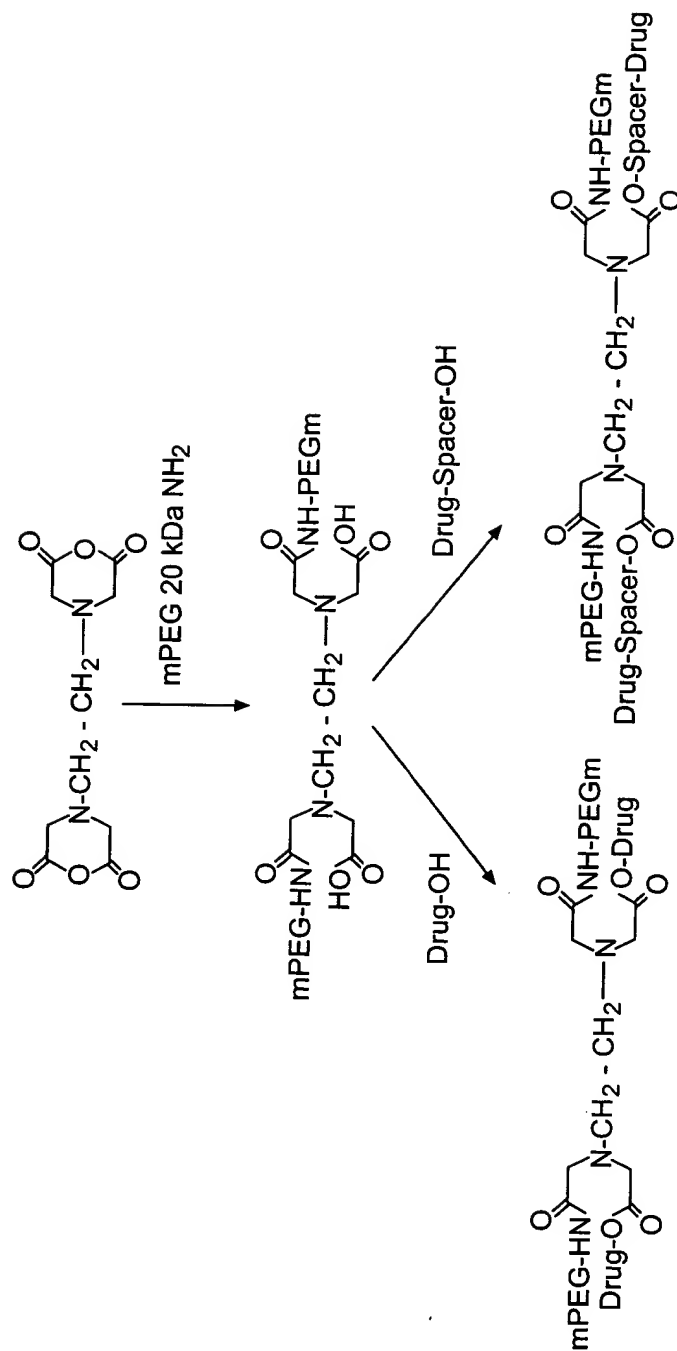


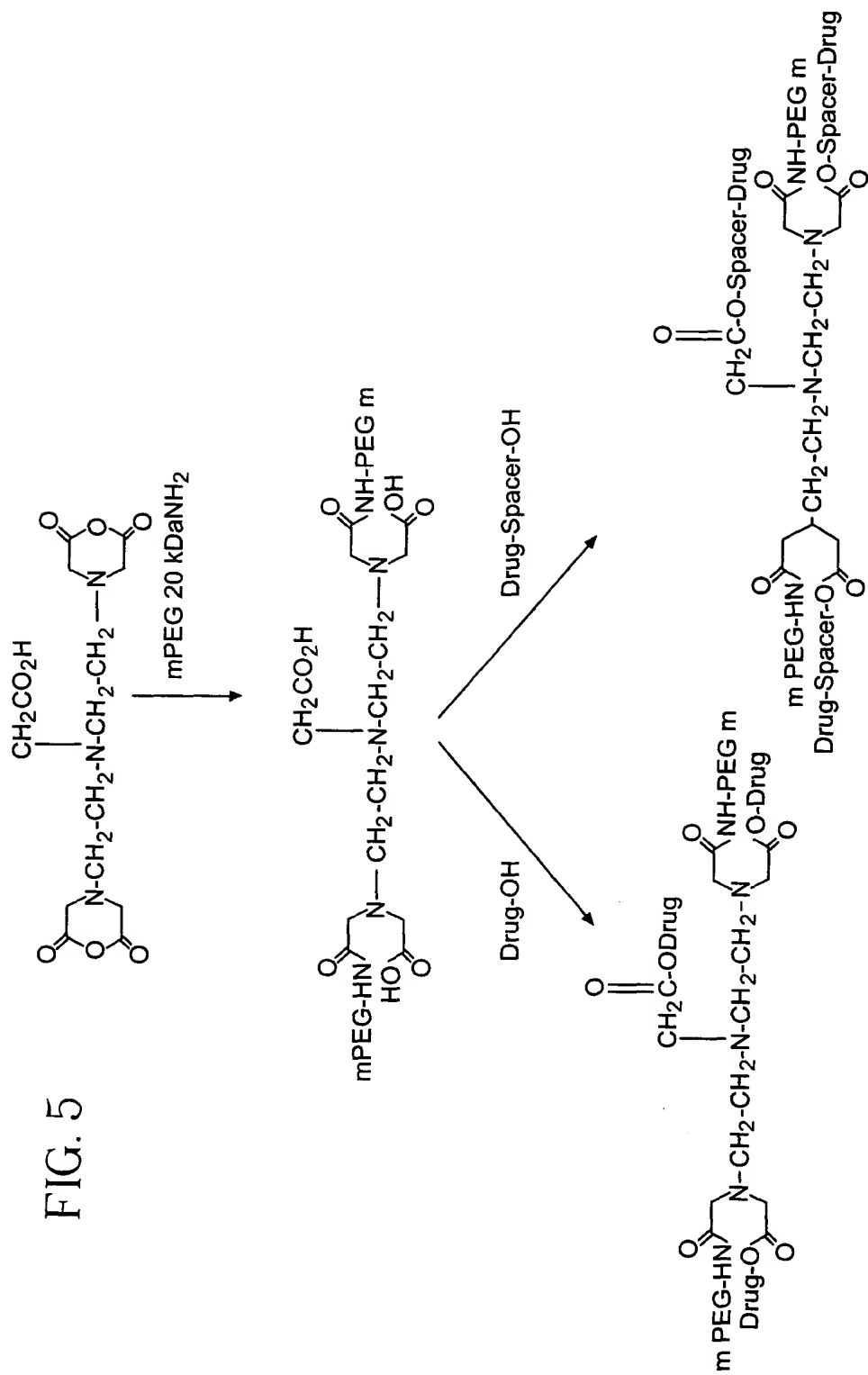
FIG. 3



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FIG. 4





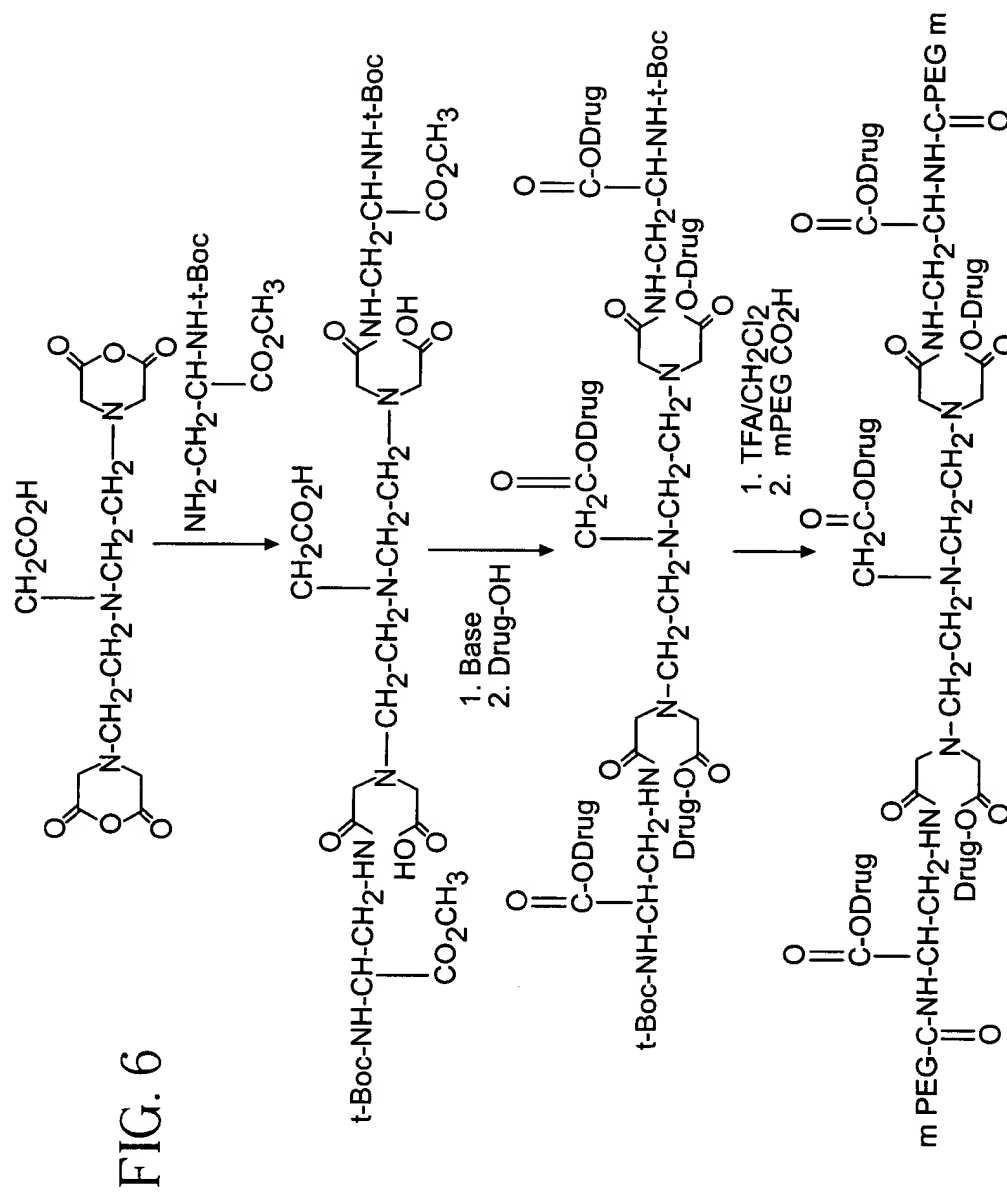


FIG. 7

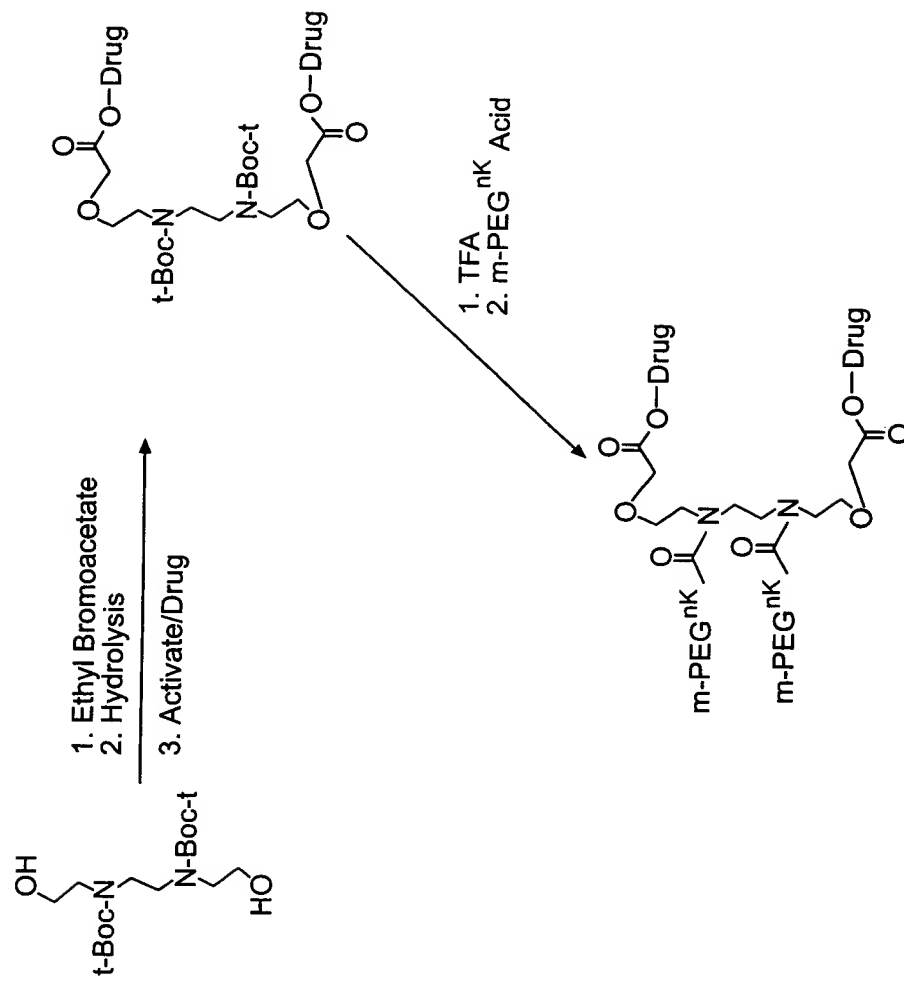


FIG. 10

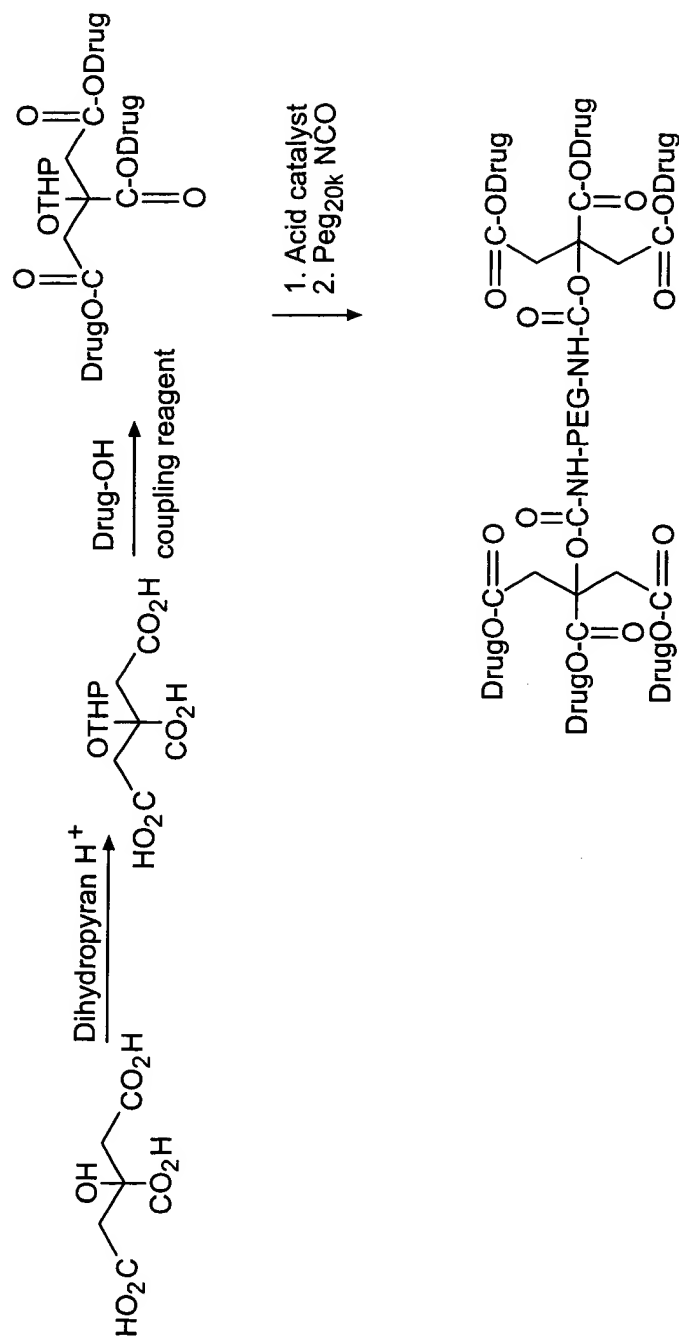
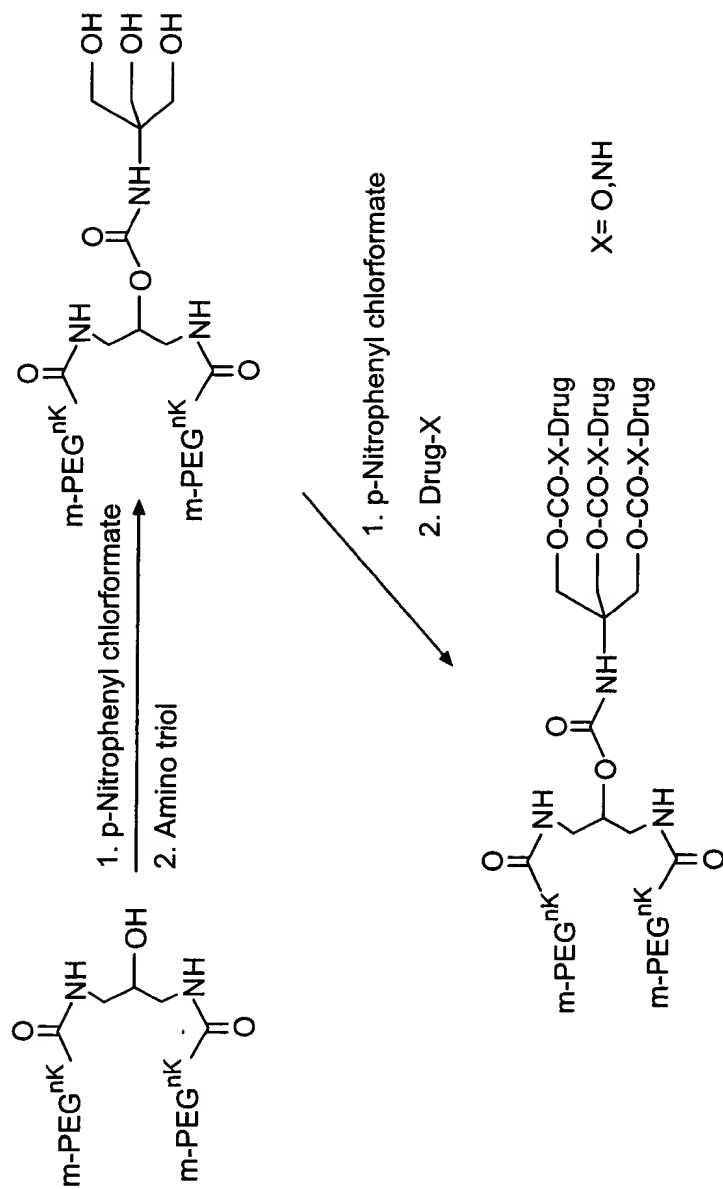


FIG. 11



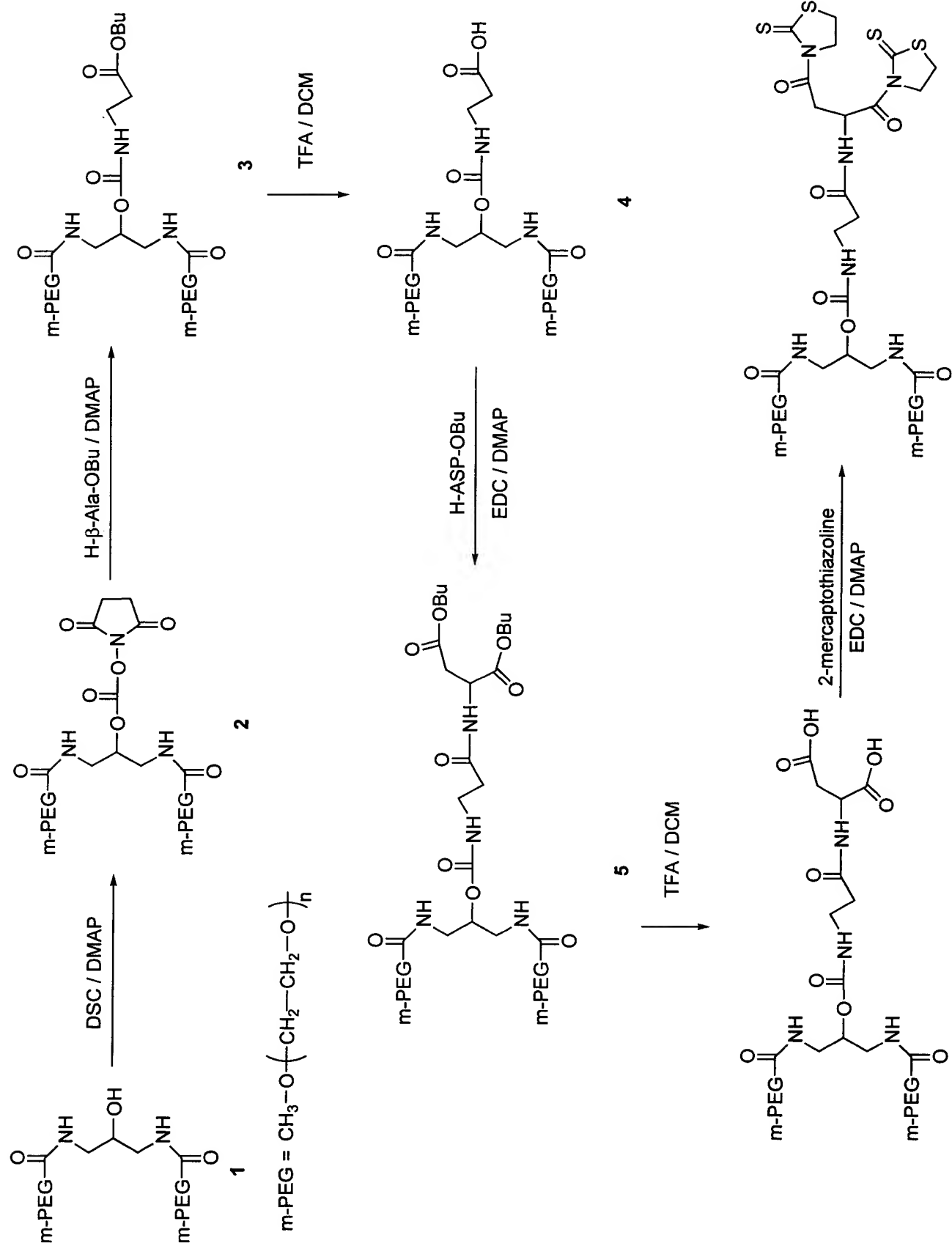


Figure 12b

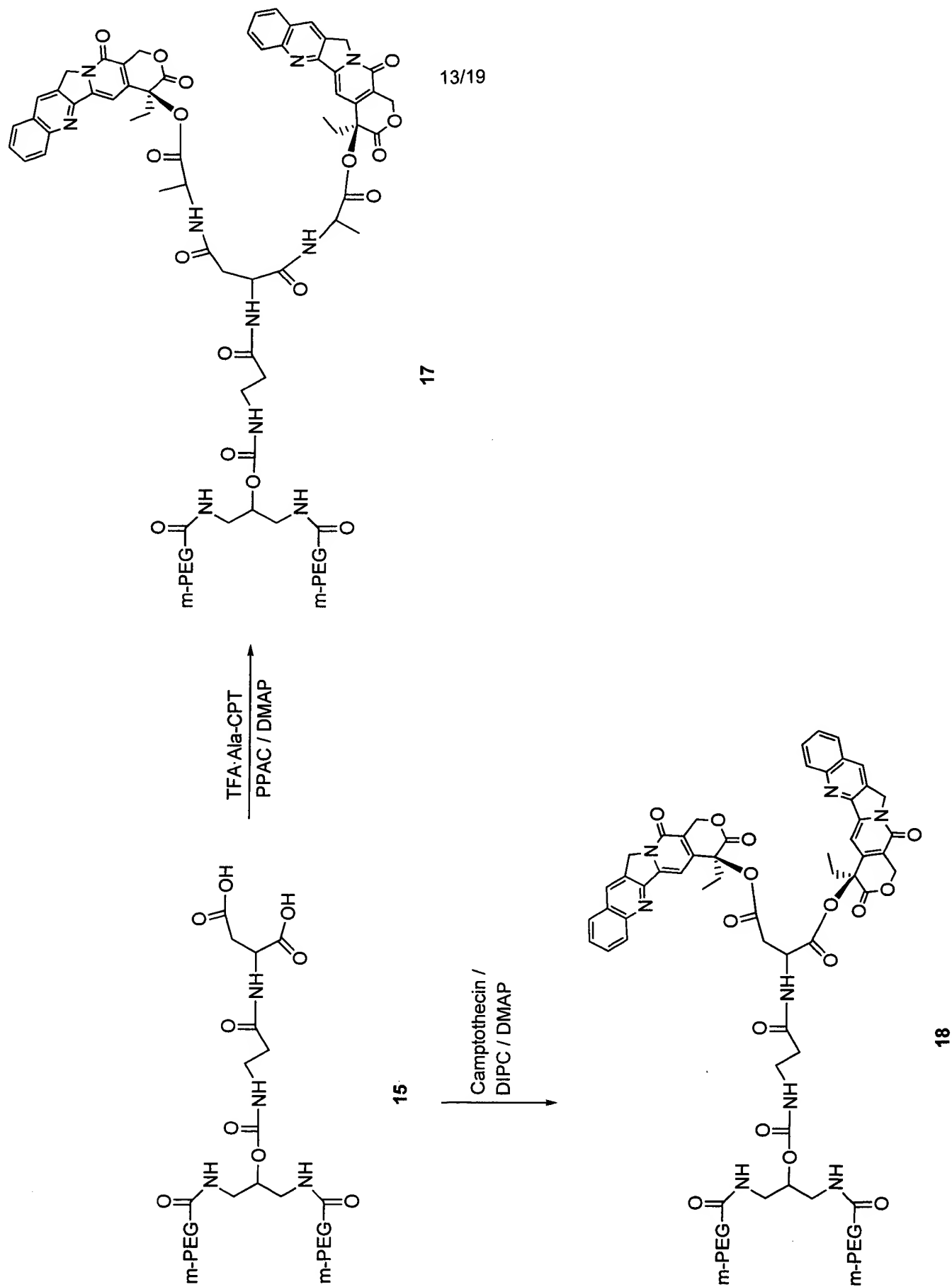


Figure 12c

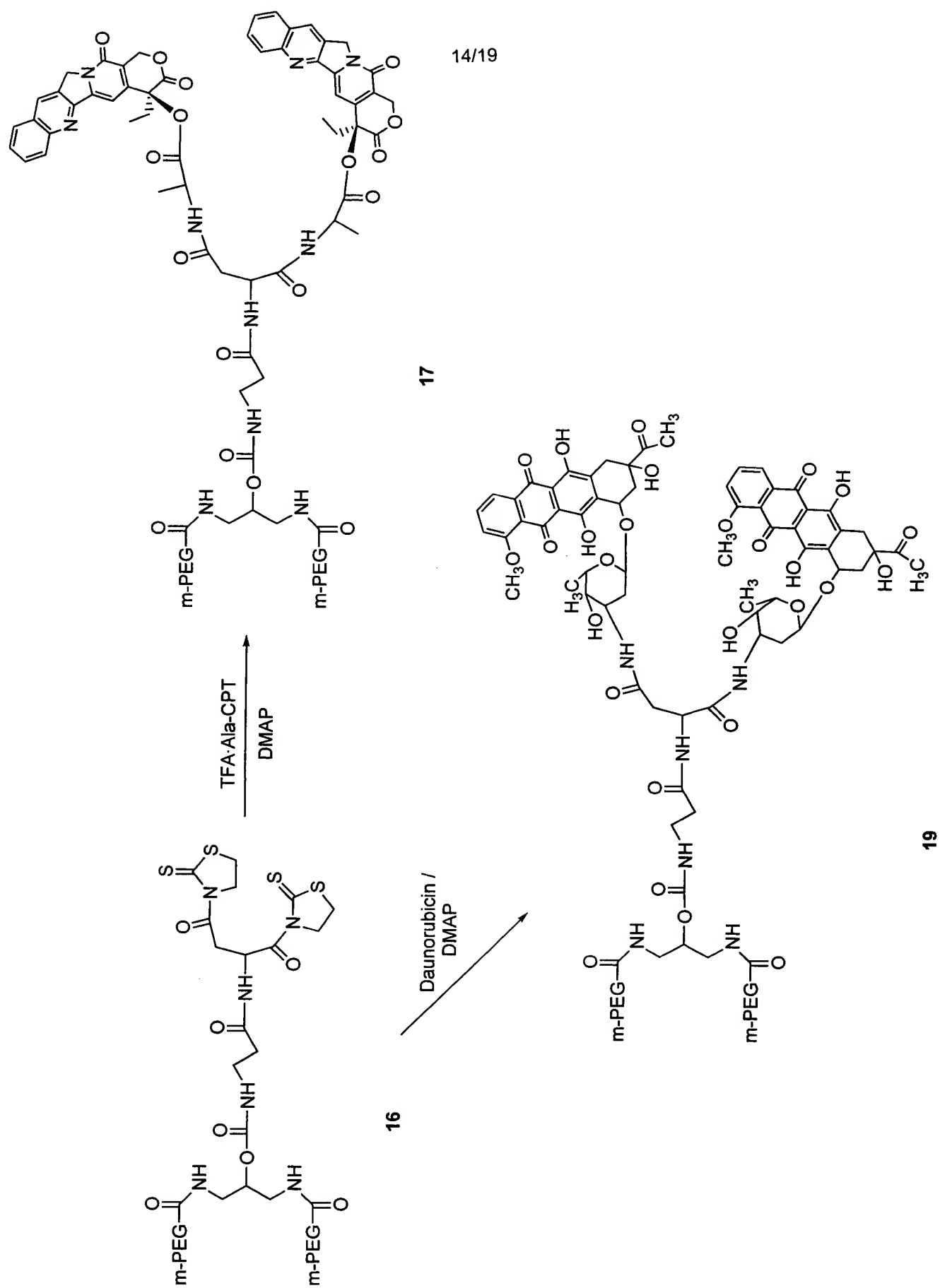


FIG. 13

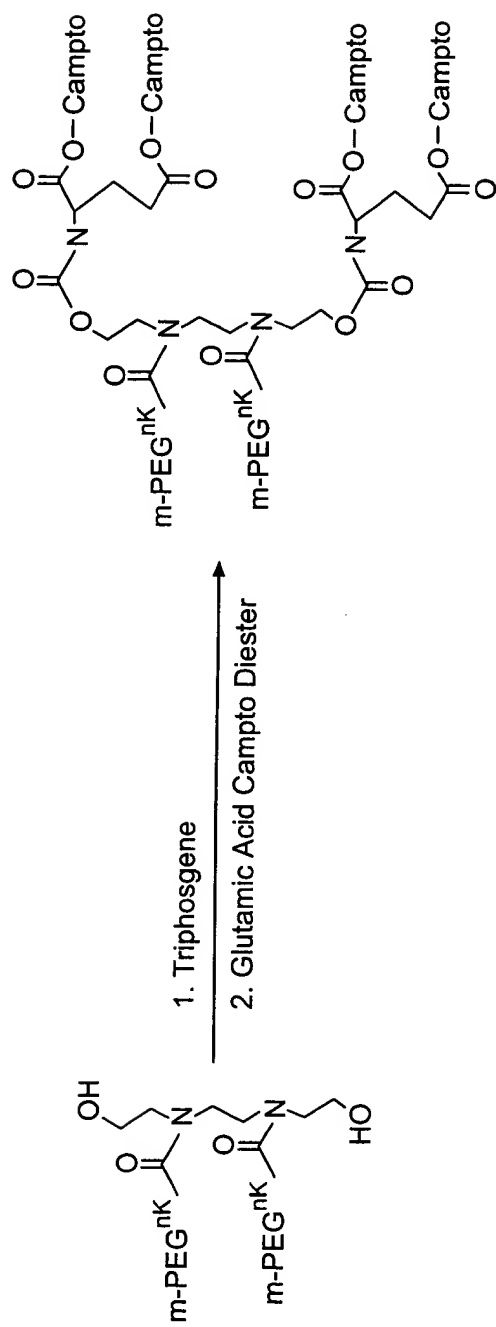


FIG. 13

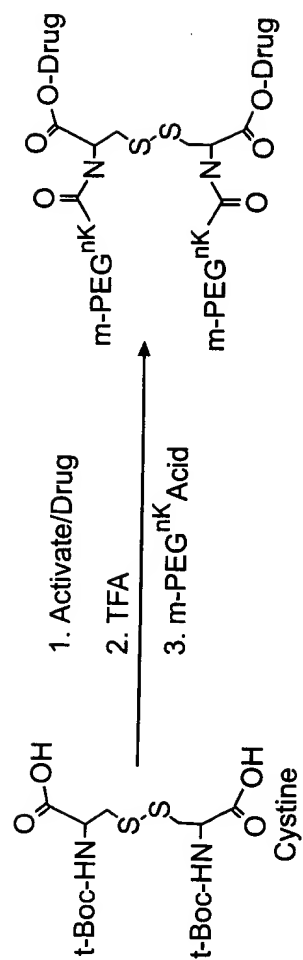
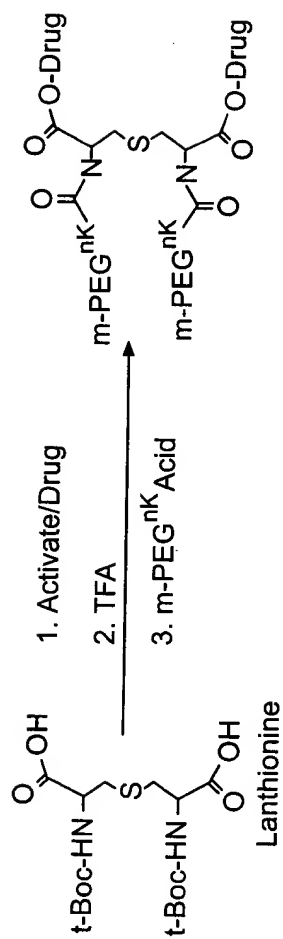


FIG. 16

